

Marked-up Version of Substituted Paragraphs

Please substitute the following paragraph at page 9, lines 15-25:

In another embodiment, MK can be used as a marker for certain types of cancers, such as hepatocellular carcinoma. Blood MK level rises with the advancement of the stage of hepatocellular carcinoma. For cancer diagnosis, the assay described above is performed multiple times sequentially[(over time)], and the change in MK level is evaluated. For example, this assay is performed over six months to a year, every twenty-four to seventy-two hours, and is performed thereafter as necessary. Generally, cancer is progressing in patients whose MK value, as detected by antibodies, is increasing sequentially[ over time].

Please substitute the following paragraph at page 14, lines 19-24:

Specifically, for rabbits, 400 µg MK containing solution mixed with an equivalent amount of Freund's complete adjuvant was initially injected subcutaneously, and from the second time and onwards, 400 µg MK containing solution mixed with an equivalent amount of Freund's incomplete adjuvant was injected each time subcutaneously. For chickens, the procedure was similar to that of rabbits, except that 100 µg MK was used each time for injections.

Marked-up Version of Substituted ClaimsClaim 1 (amended):

A method for detecting early cancer, comprising the steps of:

- a) measuring the level of midkine, [and/or] a fragment thereof, or both in a biological sample, and,
- b) comparing the measured level obtained in step a) to a [measured level]control midkine level of a healthy subject, wherein an elevated measured level as compared to the control level indicates the presence of early cancer.

Claim 9 (amended):

[A use of] A method for detecting early cancer comprising the steps of (a) contacting a biological sample with an antibody [recognizing]that specifically binds to midkine, [and/or] a fragment thereof, or both [for early cancer detection], and (b) comparing the level of binding between the antibody and midkine, a fragment thereof, or both of step (a) to a control binding level of a healthy subject, wherein an elevated binding level as compared to the control level indicates the presence of early cancer.

Claim 10 (amended):

A diagnostic agent for early cancer comprising an antibody that recognizes midkine, [and/or] a fragment thereof, or both.

Claim 11 (amended):

A kit for detecting early cancer in a biological sample, wherein (a) the kit [(a)] comprises a container that holds an antibody that specifically binds to at least one epitope of midkine, [and/or] a fragment thereof, or both and (b) the antibody determines the presence of midkine, [and/or] a fragment thereof, or both in the biological sample.

Claim 13 (amended):

A method for assessing cancer prognosis, comprising the steps of:

a) measuring the level of midkine, [and/or] a fragment thereof, or both in a biological sample, and,

b) correlating the measured level obtained from step a) to cancer prognosis, to thereby assess cancer prognosis.